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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,609	04/15/2005	Matthew A. Spear	UCSD-08833	2275

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

MAIL DATE	DELIVERY MODE
10/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,609	SPEAR, MATTHEW A.	
	Examiner	Art Unit	
	Mark L. Shibuya, Ph.D.	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Application 10501609, (20050176005 A1): Claims 1-8 are pending. Claim 7 is withdrawn form consideration. Claims 1-6 and 8 are examined.

Election/Restrictions

2. Applicant's election without traverse of the Invention of Group 1, claims 1-3 and 6-8, drawn to methods for recovering a ligand, and to the species of apoptosis, as a cellular response, and the species of Annexin V, as an indicator, in the reply filed on 8/6/2007, is acknowledged.

3. Claim 7 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species of cellular response, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/6/2007.

Priority

4. This application, 10/501,609, filed 4/15/2005, is the national stage of PCT/US03/01426, filed 1/16/2003, which claims benefit of 60/349893, filed 1/16/2002.

5. Applicant's claim to foreign priority benefit of PCT/US03/01426, filed 1/16/2003, is acknowledged. The claim to foreign priority is found in the Declaration, entered 4/15/2005.

Information Disclosure Statement

6. The information disclosure statement (IDS), submitted on 8/6/07, was considered by the examiner.

Specification

7. The amended abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new amended abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text. The direction for the amendment to the abstract, given in the amendments to the specification, entered 4/15/2005, state the "new paragraphs" should be added "[o]n a separate sheet following the claims". It is unclear as to what "separate sheet following the claims" is referred to. The examiner respectfully suggests that applicant enter the new paragraph of the abstract on a separate sheet of paper, to make the record clear.

Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential cooperative relationships of elements, such omission amounting to a gap between the necessary connections. See MPEP § 2172.01. The omitted cooperative relationships are: the relationship of "a response from at least a subset of said target cells" in lines 5-6 and "a subset of said treated target cells is activated" in line 9. It is unclear as to what the relationship is between the "response" of line 5 and the –activation-- of line 9; *i.e.*, it is unclear as to whether they are the same phenomena. Furthermore, it is unclear what the relationship of the "at least a subset of target cells", (lines 5-6), is to the "subset of treated target cells", (line 9) , i.e., it is unclear as to whether they are the same cells.

Claim 3 recites the limitation "said target cell" in line 1. There is uncertain antecedent basis for this limitation in the claim. Claim 1, upon which claim 3 depends, recites the plural "target cells" and "a detected activated target cell" and "a collected activated target cell"; it is unclear as to whether one or all of these cells are the "said target cell".

Claim 4 recites the abbreviation "ALL" in line 3. This abbreviation should be spelled out. For example, the language --acute lymphoblastic leukemia, ("ALL")-- in lines 1-2, would overcome this rejection.

Claim 6 recites the limitation "said cellular response" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Larocca, WO 99/10485.

The claims are drawn broadly to a method comprising: a) providing; i) target cells, ii) a library comprising a plurality of ligands, wherein at least one ligand is capable of binding so as to cause a response from at least a subset of said target cells, and iii) an indicator; b) contacting the target cells with said ligands of said library to create treated target cells, under conditions such that a subset of said treated target cells is activated; c) exposing said treated target cells to said indicator, under conditions such

that the at least one activated target cell is detected to create a detected activated target cell; d) collecting said detected activated target cell to create a collected activated target cell; and e) recovering said ligand from said collected activated target cell; and variations thereof.

Larocca, WO 99/10485, throughout the publication, and at pp. 2-3, pp. 10-13, discloses methods comprising providing target cells, a library of ligand and an indicator; contacting the target cells with the ligands of the library to create treated target cells that are activated; exposing the treated cells to the indicator, collecting the activated target cell and recovering the ligand from a collected activated target cell. Larocca teaches cell uptake, which reds on a cellular response. Larocca, at p. 10, lines 19-26, teach that test cells may be any cells that express a receptor of choice or are a cell type or source for which gene therapy is destined. Larocca at p. 10, lines 27-33, teach selecting for tumor-specific ligands. Larocca, at p. 11, teach reporter gene products, reading on an indicator, and detection by fluorescence microscopy or flow cytometry. Larocca, at p. 15, lines 20-28, teach lymphomas as among those tumors amenable for treatment by phage. Larocca, at pp. 22-23, Examples 9 and 10, teach screening a phage library against a target tissue or cell line, in order to obtain ligands against the target cell. Larocca at e.g., p. 26, discloses panning as a screening procedure that is known in the art.

12. Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Larocca et al., U.S. 6,472,146 B1.

Larocca, throughout the patent, and at col. 2, discloses methods comprising providing target cells, a library of ligand and an indicator; contacting the target cells with the ligands of the library to create treated target cells that are activated; exposing the treated cells to the indicator, collecting the activated target cell and recovering the ligand from a collected activated target cell. Larocca, at col. 8, teach that test cells may be any cells that express a receptor of choice or are a cell type or source for which gene therapy is destined. Larocca at col. 8, teach selecting for tumor-specific ligands. Larocca, at col. 11, teach detection by fluorescence microscopy or flow cytometry. Larocca, at col.s 14-15, teach lymphomas as among those tumors amenable for treatment by phage. Larocca, at Examples 9-12, teach screening a phage library against a target tissue or cell line, in order to obtain ligands against the target cell. Larocca at e.g., col. 1, discloses panning as a screening procedure that is known in the art.

13. Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Spear et al., Cancer Gene Therapy, July 2001, Vol. 8, No. 7, pp 506-511, (IDS 8/6/2007, Cite No. 8).

Spear et al., throughout the publication, disclose methods comprising providing target cells that are cancer cells, a library of ligand and an indicator detectable by

enzyme-linked immunosorbent assay (ELISA); contacting the target cells with the ligands of the library to create treated target cells that are activated; exposing the treated cells to the indicator, collecting the activated target cell and recovering the ligand from a collected activated target cell.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1-6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Larocca, **WO 99/10485**, Larocca et al., U.S. **6,472,146 B1**; and **Spear** et al., Cancer Gene Therapy, July 2001, Vol. 8, No. 7, pp 506-511, (IDS 8/6/2007, Cite No. 8); each taken separately and each separately in view of **Ebner** et al., US 6,495,520 B2.

The prior art references of Larocca, WO 99/10485, Larocca et al., U.S. 6,472,146 B1; and Spear et al., Cancer Gene Therapy, July 2001, Vol. 8, No. 7, pp 506-511, (IDS 8/6/2007, Cite No. 8), are relied as in the above rejections under 35 U.S.C. 102.

The prior art references of Larocca, WO 99/10485, Larocca et al., U.S. 6,472,146 B1; and Spear et al., Cancer Gene Therapy, July 2001, Vol. 8, No. 7, pp 506-511, (IDS 8/6/2007, Cite No. 8), do not disclose methods comprising acute lymphoblastic leukemia (ALL) cells, (in culture or from the patient) and a cellular response that is apoptosis and wherein the indicator comprised fluorescent-labeled Annexin V.

Ebner et al., US 6,495,520 B2, throughout the patent, and col.s 47-50, teach methods for identifying agonist compounds of Apoptosis Inducing Molecule II (AIM II), including antibodies selected by phage display. Ebner et al., at col. 51, teach the targeting of ALL cells, and at col.s 83-84, teach assaying for apoptosis of Jurkat tumor cells by Annexin V-FITC FaCScan flow cytometry, in order to show retroviral transduction of the AIM II gene into MDA-MB-231 or MC-38 cells.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used methods for detecting ligands from activated target cells comprising acute lymphoblastic leukemia (ALL) cells, (in culture or from the patient) and a cellular response that is apoptosis and wherein the indicator comprised fluorescent-labeled Annexin V.

One of ordinary skill in the art would have been motivated to make and use methods for detecting ligands from activated target cells comprising acute lymphoblastic leukemia (ALL) cells, (in culture or from the patient) and a cellular response that is

apoptosis and wherein the indicator comprised fluorescent-labeled Annexin V, because Ebner et al., teaches that ALL cells, apoptosis and indicator comprised fluorescent-labeled Annexin V, were familiar in the art; the methods of combining these elements were familiar in the art; and the results of combining these elements would have been predictable. Furthermore, one of ordinary skill in the art would have been motivated to use methods of recovering ligands that induce apoptosis in cancer cells, such as ALL, in order to find ligands that would kill those cancer cells in the course of cancer therapy.

Conclusion

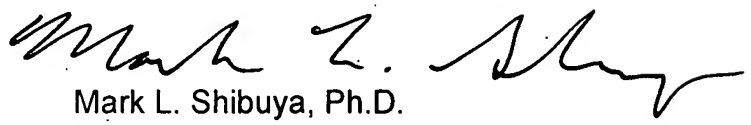
16. Claims 1-6 and 8 are rejected.

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Spear et al., HSV-1 Amplicon Peptide Display Vector, J. Virological Methods (2002), Vol. 107, pp. 71-79.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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Art Unit 1639